HAUTE AUTORITÉ DE SANTÉ

DERMATOLOGY
New indication
March 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

STELARA (ustekinumab), immunosuppressive interleukin inhibitor

No demonstrated clinical benefit in the management of severe chronic plaque psoriasis in adolescents

Main points

- STELARA now has marketing authorisation in the treatment of moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.
- It should be reserved for treatment of chronic and severe plaque psoriasis defined by:
  - failure (insufficient response, contraindication or intolerance) to at least two treatments including nonbiologic systemic treatments and phototherapy
  - an extensive form and/or substantial psychosocial impact.
- The safety profile of ustekinumab is similar in adults and adolescents.

Pre-existing indications[i]

STELARA already has marketing authorisation in the same psoriasis treatment indication but in adults and in the treatment of psoriatic arthritis.

Therapeutic use

- In both children and adults, treatments for mild forms of plaque psoriasis are local: first-line topical steroids and vitamin D3 analogues (only calcitriol has marketing authorisation in children). Moisturising the skin with emollients is often combined with topical treatments.
  Moderate to severe forms not sufficiently responding to topical treatments are treated with systemic treatments: acitretin (retinoid), cyclosporine and methotrexate (off-label in children) or phototherapy in adolescents. Due to their toxicity, the use of these treatments must be of limited duration. Anti-TNFα, etanercept (ENBREL, from 6 years of age) and adalimumab (HUMIRA from 4 years of age), and IL-12/23 inhibitor ustekinumab (STELARA, from 12 years of age) are last resort treatments in severe forms.
- These treatments do not permanently cure the condition, but provide transient, more or less complete resolution of the lesions and the therapeutic strategy is rotational particularly due to diminishing response.
- **Role of the medicinal product in the therapeutic strategy**
  In adolescents from 12 years of age, STELARA is a second-line treatment in the treatment of chronic and severe plaque psoriasis defined by:
  - failure (insufficient response, contraindication or intolerance) to at least two treatments including nonbiologic systemic treatments and phototherapy
  - and an extensive form and/or substantial psychosocial impact.

Clinical data

- Ustekinumab was compared to placebo in a randomised, double-blind study in adolescents aged 12 to 17 years with moderate to severe plaque psoriasis who failed local treatments.
  Among the patients included, 43% had prior conventional systemic treatment, 42% with phototherapy and 11% with biologics.

[i] This summary does not cover these indications.

Ustekinumab (at the marketing authorisation dosage) was superior to placebo at week 12 on the percentage of PGA (Physician Global Assessment responders [primary endpoint]) 0 (clear) or 1 (almost clear): 69.4 % *versus* 5.4 % ($p < 0.001$).
It was also superior to placebo on the secondary endpoints PASI 75 (80.6 % *versus* 10.8%, $p< 0.001$) and PASI 90 (61.1% *versus* 5.4%).
There are no specific data available in adolescents who failed systemic treatments or data *versus* etanercept.

- The safety profile of ustekinumab in adolescents is comparable to that observed in adults in this indication. Two new risks were identified according to pharmacovigilance data. The incidence of the main risks, i.e., serious infections, malignant tumours and major cardiovascular events, did not increase and severe hypersensitivity reactions were rare.

Special prescribing conditions

- Medicine for initial hospital prescription.
- Prescription restricted to specialists in dermatology, rheumatology or internal medicine.
- Exception drug status

Benefit of the medicinal product

- The actual benefit* of STELARA is substantial only in the treatment of severe chronic plaque psoriasis in adolescents from 12 years of age, defined by:
  - failure (insufficient response, contraindication or intolerance) to at least two treatments including nonbiologic systemic treatments and phototherapy
  - and an extensive form and/or substantial psychosocial impact.
- STELARA provides no improvement in clinical added value** (CAV V) in the management of severe chronic plaque psoriasis as defined above.
- Recommends inclusion on the list of reimbursable products for supply by retail pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 16 March 2016 (CT-14846) available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".